REMARKS

Claims 1-31 are pending in this case. Claims 1-14 stand rejected and Claims 15-31 were withdrawn from consideration by the Examiner by a restriction requirement in a non-final office action mailed January 26, 2007.

With this proposed amendment, Applicants request that independent claim 1 be amended and the Examiner's consideration of the remarks presented herein. Further, in view of the claim amendment and Applicants remarks, Applicants respectfully request the Examiner's consideration and allowance of claims 1-14.

Amended Claim

Amended independent claim 1 is presented for the Examiner's consideration. The amendment of claim 1 corrects the typographical error of a missing unit after "2.0" by adding "kP" and adds the limitation that the water soluble excipient and low melting point compound are a fast dissolve granulation. The addition of this limitation is supported, for example, by paragraph 44 of Applicants' specification which describes and defines "fast dissolving granulation". Paragraph 44 in relevant part is provided below for the Examiner's reference.

> A preferred method of forming the tablet compositions of the invention includes preparing a fast dissolving granulation by mixing a low-melting point compound, (preferably a hydrogenated oil, partially hydrogenated oil or hydrogenated oil derivative) and a water soluble excipient, (preferably a saccharide or modified saccharide). The term "fast dissolving granulation" refers to a composition of the low melting point compound and the water soluble excipient prepared for use as a granulation in the manufacture of tablets of the invention. A portion of the fast dissolving granulation may then be added to the remaining ingredients.

Applicants have also added the limitation in the preamble that the tablet is a "non-effervescent" tablet which is supported, for example by paragraph 7 of Applicants' specification.

Applicants believe that this amended claim further points out and distinguishes Applicants' invention. As claims 2-14 variously depend from claim 1, the amendment likewise applies to dependent claims 2-14. Applicants respectfully request that the Examiner consider this proposed amendment and allow amended independent claim 1 and claims 2-14 which variously depend from claim 1.

Inventorship

The Examiner notes that the Application currently names joint inventors and presumes correctly that the subject matter of the various claims was commonly owned at the time of the inventions covered therein.

Rejection Under 35 USC §112

The Examiner has rejected claim 1 as being indefinite as no unit of measurement is associated with the phrase "a hardness of about 2.0 or lower". The omission of the unit in the claim was a typographical error. Accordingly, claim 1 has been amended to add the unit of measure "kP". This amendment is supported, for example, by paragraph 11 of the specification.

Applicants' believe that this amendment provides the clarification requested by the Examiner and respectfully request the rejection of claim 1 as indefinite under 35 USC §112 be withdrawn.

Rejection Under 35 USC §102 - Wehling

Claims 1-5, 7-10 and 13 stand rejected under 35 USC §102 (b) as being anticipated by Wehling etal (U.S. 5,178,878, herein "Wehling"). Wehling is directed to a pharmaceutical dosage form that comprises microparticles combined in a tablet

with an effervescent disintegration agent (see abstract of Wehling). Column 5 line 51-Col. 6 line 66 of Wehling describe in detail that Wehling's invention requires an effervescent disintegration agent (e.g. a compound that can evolve gas), and that it is the effervescent agent that promotes the "rapid and complete" disintegration of the tablet. Accordingly Wehling teaches both that an effervescent agent is necessary for rapid disintegration of the tablet and that the effervescent agent is the component responsible for the rapid disintegration of the tablet.

Applicant's invention neither requires nor describes an effervescent agent. Applicant's invention utilizes a fast dissolving granulation prepared by mixing a low melting point compound and a water soluble excipient, for example, a saccharide. The fast dissolve granulation, not an effervescent agent or gas forming component, facilitates the rapid disintegration of Applicants' invention.

The Examiner cites listings in Wehling of lubricants (col. 9, lines 8-20) and water soluble excipients (col 7., lines 35-51 and Example I). The listing of lubricants is a general listing of lubricants. There is no teaching that either a lubricant must be used or any teaching other than the use of lubricants in the manufacture of effervescent tablets. Namely, Wehling Col. 8, lines 40-41 states that "lubricants are *normally* used in the manufacture of effervescent tablets." Further, the listing of lubricants cited by the Examiner includes liquids (such as mineral oil) and solids (such as sodium benzoate - m.p.300°C and magnesium oxide – m.p2800°C) which have melting points substantially above 37°C.

Accordingly, there is no teaching or suggestion in Wehling that a low melting point compound that melts below 37°C is needed or required or that such a component in combination with a water soluble excipient forms a fast dissolving granulation.

The Examiner cites col. 7, lines 35-51 as disclosing water soluble excipients. In the paragraph immediately before the list cited by the Examiner, Wehling discloses that the Wehling's invention "*may* further include one or more additional adjuvants which can be chosen from those known in the art including flavors, dilutents, colors, binders, filler, compaction vehicles, and non-effervescent disintegrants." Further, col.

7 line 35 cited by the Examiner begins with "Example of binders which can be used include..." and includes not only a number of compounds including sugars which do dissolve in water, but also other compounds such as gum acacia and guar gum, for example, which are more properly characterized as dispersing in water not dissolving.

Thus, Wehling neither teaches that a water soluble excipient as disclosed by Applicants is required or that a water soluble excipient in combination with a low melting point solid forms a fast dissolving granulation.

In view of at least these distinctions and the fact that Applicants have amended independent Claim 1 to specify that the water soluble excipient and low melting point compound are a fast dissolve granulation, Applicants respectfully request that the Examiner withdraw the rejection of claims 1-5, 7-10 and 13 as anticipated under 35 USC §102 (b) by Wehling et al.

Rejection Under 35 USC §102 - Mizumoto

Claims 1,4,5, 7-9 and 14 stand rejected as anticipated by Mizumoto et al. (U.S. 5,576,014, herein "Mizumoto") which the Examiner characterizes as an intrabuccally dissolving compressed molding. Mizumoto teaches a composition that achieves the desired dissolution properties by combining low moldability and high moldability saccharides (see col. 5., lines 60-67 and Claim 1). Further, the Examiner cites Mizumoto col. 6 lines 37-46 for the statement that "these saccharides may be used alone or in combination". The paragraph that the Examiner cites is descriptive of the "saccharide having low moldability" which as lines 45 and 46 state may be a single saccharide or a mixture of two or more of "these saccharides". The paragraph immediately following the one cited by the Examiner, i.e. col. 6 lines 47-55, provides a parallel description of the " a saccharide having high moldability" and that a single saccharide having high moldability or a mixture of such saccharides may be used.

Accordingly, Mizuumoto clearly sets forth that the desirable features of the Mizomoto composition are derived from combining at least one of a "high moldability saccharide" and at least one of a "low moldability saccharide".

Accordingly, in contrast to applicants' invention, Mizumoto neither teaches that *a* water soluble excipient is required (Mizumoto requires at least two saccharides with specified moldabilities) or that a water soluble excipient in combination with a low melting point solid forms a fast dissolving granulation.

The Examiner cites column 13, lines 50-65 for a listing of lubricants. The listing of lubricants is a general listing of lubricants. There is no teaching that a lubricant must be used as in col. 13 lines 32-35, Mizumoto states that the invention *"may contain"* other additives which include lubricants (see col. 13, lines 32-35). Further, of the lubricants listed in Mizumoto, magnesium stearate, talc and stearic acid have melting points substantially above 37°C (see standard references for melting points such as for example, Merck index). The other two lubricants listed by Mizumoto are classes of compounds (i.e., sucrose esters and polyethylene glycols) which have a range of melting points that include members in each class that have melting points above 37°C. Accordingly, there is no teaching in Mizomoto that a low melting point compound that melts below 37°C is needed or required or that such a component in combination with a water soluble excipient forms a fast dissolving granulation.

In view of at least these distinctions and the fact that Applicants have amended independent Claim 1 to specify that the water soluble excipient and low melting point compound are a fast dissolve granulation, Applicants respectfully request that the Examiner withdraw the rejection of claims 1,4,5, 7-9 and 14 as anticipated under 35 USC §102 (b) by Mizumoto et al.

Rejection Under 35 USC §102 (e) - Shimizu

Claims 1,4,5, 7-9 and 14 stand rejected as anticipated by Shimizu et al. (U.S. 6,299,904 B1, herein "Shimizu"). As the Examiner states, Shimizu teaches a composition comprising a pharmaceutically active ingredient, one or more sugar alcohols selected *from the group consisting of* sorbitol, maltitol, reduced starch saccharide, xylitol , reduced papatinose and erythritol, and a hydroxproypyl cellulose.

First Shmizu does not generally disclose saccharides but a very specific list of sugar alcohols from which the saccharide must be selected. In paragraph 30

Applicants disclose a lengthy list of suitable water soluble excipients including a number of mono and disaccharides, artificial sweeteners and amino acids. Further Applicants' indicate in paragraph 30 that the monoaccharide mannitol is a preferred saccharide. Shimizo does not even list mannitol. (Note that maltitol, which is listed by Shimizu, is defined by Dorland's On-Line Medical Dictionary as a hydrogenated, partially hydrolyzed starch used as a bulk sweetener – a very different substance than the disaccharide mannitol).

Secondly, Shimzu discloses a combination of one or more of a limited number of sugar alcohols with a very hydroscopic material hydroxypropylcellulose. Shimizu does not teach a fast dissolving granulation of a water soluble excipient in combination with a low melting point solid.

The Examiner cites column 6, lines 26-34 for a listing of lubricants. The listing of lubricants is a general listing of lubricants. There is no teaching that a lubricant must be used as in col. 5, lines 51-60, Shimzuo states that the invention "*may further contain*" other additives which include lubricants. Further, of the lubricants listed in Shmizu, magnesium stearate, talc and stearic acid have melting points substantially above 37°C. The other two lubricants listed by Shimzu are classes of compounds (i.e., sucrose esters and polyethylene glycols) which have a range of melting points that include members in each class that have melting points above 37°C. Accordingly, there is no teaching in Shimzu that a low melting point compound that melts below 37°C is needed or required or that such a component in combination with a water soluble excipient forms a fast dissolving granulation.

In view of at least these distinctions and the fact that Applicants have amended independent Claim 1 to specify that the water soluble excipient and low melting point compound are a fast dissolve granulation, Applicants respectfully request that the Examiner withdraw the rejection of claims 1,4,5, 7-9 and 14 as anticipated under 35 USC §102 (e) by Shimzu et al.

Rejection Under 35 USC §103 – Wehling in view of Mauger

Claims 1-14 stand rejected under 35 USC §103 over Wehling et al. (US 5,178,878) in view of Mauger et al. (US 5,728,403, herein "Mauger"). As discussed

in detail above, Wehling is directed to a pharmaceutical dosage form that comprises microparticles combined in a tablet with an effervescent disintegration agent (see abstract of Wehling), and teaches both that an effervescent agent is necessary for rapid disintegration of the tablet and that the effervescent agent is the component responsible for the rapid disintegration of the tablet. Further, there is no teaching that either a lubricant must be used or that a low melting point compound must be used as Wehling's general list of optional lubricants includes high melting point solids such as sodium benzoate - m.p.300°C and magnesium oxide – m.p.2800°C) which have melting points substantially above 37°C.

Applicant's invention neither requires nor describes and effervescent agent. Applicant's invention utilizes a fast dissolving granulation prepared by mixing a low melting point compound and a water soluble excipient, preferably a saccharide. The fast dissolve granulation, not an effervescent agent or gas forming component, facilitates the rapid disintegration of Applicants' invention.

Thus, Wehling neither teaches or suggests that a water soluble excipient and a low melting point compound is required or that a water soluble excipient in combination with a low melting point solid forms a fast dissolving granulation. Wehling also does not provide a reasonable expectation of success because Wehling teaches a fast dissolving tablet based on a gas forming chemical reaction and does not suggest other alternatives.

The deficiencies of Wehling are not cured by Mauger. Mauger is directed to a taste masking coating not to a tablet that dissolves readily (see abstract, column 1, lines 56-65 and claim 1). In fact the coating is a mixture of triglycerides and a polymer with the coating intended to remain intact until the tablet reaches the stomach (col. 2 lines 21-29). Arguably Mauger doesn't even teach a fast dissolve coating much less a fast dissolve tablet. Mauger teaches the use of low melting point compounds in combination with a polymer to form a coating that remains intact until the tablet gets to the stomach. Thus Mauger neither teaches or suggests the elements needed to cure the identified deficiency of Wehling - namely the combination of a water soluble excipient and a low melting point solid that forms a fast dissolving granulation.

In order to make a showing of obviousness, the Examiner must make the four factual inquiries set forth in *Graham v. John Deere*, 383 U.S. 1, 17-18 (U.S. 1966): (1) determining the scope and content of the prior art; (2) ascertaining the differences between the prior art and the claims at issue; (3) resolving the level of ordinary skill in the pertinent art; and (4) evaluating evidence of secondary considerations, such as long felt need, commercial success, and unexpected results. *See KSR Int'l Co. v. Teleflex, Inc.*, 127 S.Ct. 1727, 1734, 167 L.Ed.2d 705, 715 (2007). The Court also stated that there is "no necessary inconsistency between the idea underlying the TSM [teaching, suggestion, or motivation] test and the Graham analysis" and that the test can provide "helpful insight" as to obviousness. *KSR*, 127 S.Ct. at 1731. Consistent with *KSR*, the Court of Appeals for the Federal Circuit recently held that in cases involving new chemical compounds, "it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound." *Takeda Chemical Industries, Ltd. v. Alphapharm Pyt, Ltd.*, No. 06-1329 (Fed. Cir. June 28, 2007), page 10.

There is no teaching or suggestion in Wehling, Mauger or in the combination of Wehling and Mauger of Applicants' invention of a combination of a water soluble excipient and low melting point to form a fast dissolving granulation or any motivation to pursuer such a composition.

In view of at least these distinctions and the fact that Applicants have amended independent Claim 1 to specify that the water soluble excipient and low melting point compound are a fast dissolve granulation, Applicants respectfully request that the Examiner withdraw the rejection of claims 1- 14 under 35 USC §103 over Wehling et al. (US 5,178,878) in view of Mauger et al. (US 5,728,403).

Rejection Under 35 USC §103 – Mizumoto in view of Mauger

Claims 1-14 stand rejected under 35 USC §103 over Mizumoto et al. (US 5,576,014) in view of Mauger et al. (US 5,728,403 , herein "Mauger"). As discussed in detail above, Mizumoto teaches a composition that achieves the desired dissolution properties by combining low moldability and high moldability saccharides

(see col. 5., lines 60-67 and Claim1). Mizumoto clearly sets forth that the desirable features of the Mizomoto composition are derived from combining at least one of a "high moldability saccharide" and at least one of a "low moldability saccharide" (Col. 5 lines 12-67)

In contract to Applicants' invention, Mizumoto neither teaches nor suggests that *a* water soluble excipient is required (Mizumoto requires at least two saccharides with specified moldabilities) or that a water soluble excipient in combination with a low melting point solid forms a fast dissolving granulation. Mizumoto provides no suggestion or motivation to substitute a low modability saccharide or a high moldability saccharide with a low melting point compound. Mizumoto stresses the importance of having both a low and high moldability saccharides present and teaches that that they should be granulated together to get the best characteristics of each (col. 5, lines 52-66). By way of contrast, in accordance with the present invention, it makes no difference whether the water soluble excipient such as a saccharide is "low molding" or "high molding".

As discussed above, the listing of lubricants in Mizumoto is a general listing of optional lubricants. Further, of the lubricants listed in Mizumoto in column 13, lines 50-65, magnesium stearate, talc and stearic acid have melting points substantially above 37°C. The other two lubricants listed by Mizumoto are classes of compounds (i.e., sucrose esters and polyethylene glycols) which have a range of melting points that include members in each class that have melting points above 37°C. Accordingly, there is no teaching or suggestion in Mizomoto of a low melting point compound that melts below 37°C in combination with a water soluble excipient that forms a fast dissolving granulation.

Mizumoto also does not provide a reasonable expectation of success combining a low melting point compound with a water soluble excipient to form a fast dissolve granulation. Mizumoto focuses on achieving a compression molded formulation showing quick disintegration and fast dissolution by inclusion of granules comprising at least two sacchardies – one with low moldability properties and one with high moldability properties.

The deficiencies of Mizumoto are not cured by Mauger. Mauger is directed to a taste masking coating not to a tablet that dissolves readily (see abstract, column 1, lines 56-65 and claim 1). As discussed above, the coating is a mixture of triglycerides and a polymer with the coating intended to remain intact until the tablet reaches the stomach (col. 2 lines 21-29), and arguably, Mauger doesn't even teach a fast dissolve coating much less a fast dissolve tablet. Mauger teaches the use of low melting point compounds in combination with a polymer to form a coating that remains intact until the tablet gets to the stomach. Thus Mauger neither teaches or suggests the elements needed to cure the identified deficiency of Mizumoto - namely the combination of a water soluble excipient and a low melting point solid that forms a fast dissolving granulation.

Thus, there is no teaching, suggestion in Mizumoto, Mauger or in the combination of Mizumoto and Mauger of Applicants' invention of a combination of a water soluble excipient and low melting point to form a fast dissolving granulation. Or any motivation to from Applicants' fast dissolve granulation.

In view of at least these distinctions and the fact that Applicants have amended independent Claim 1 to specify that the water soluble excipient and low melting point compound are a fast dissolve granulation, Applicants respectfully request that the Examiner withdraw the rejection of claims1-14 under 35 USC §103 over Mizumoto et al. (US 5,178,878) in view of Mauger et al. (US 5,728,403).

Rejection Under 35 USC §103 – Korab in view of Mauger

Claims 1-14 stand rejected under 35 USC §103 over Korab (U.S. 4,704,269, herein "Korab") in view of Mauger. Korab is directed to an effervescent composition (see, for example, abstract and claim 1). As set forth in column 2, lines 15-20, the composition of Korab is an antacid and analgesic powder that is preferably "sucrose and sodium free" but which produces visible carbon dioxide effervescence when placed in water". As Korab states in Column 6, lines 28-33, "the effervescence aids in breaking up the tablets". There is no teaching or suggestion of any other mechanism for achieving the fast dissolve property and no teaching or suggestion

of combining a water soluble excipient and a low melting point compound to form a fast dissolving graduation.

The Examiner cites column 5, lines 20-68 for a listing of lubricants. First, the lubricants are indicated to be optional as lines 43-45 state that if the composition is to be tableted, "the formulation may include any one or more of the conventional ingredients". Secondly, of the lubricants listed some such as, for example, talc and magnesium stearate have melting points substantially above 37°C. The Examiner acknowledges on page 13 of the Office Action of 1/26/2007 that Korab does not teach a mixture including certain low melting point compounds. However, Applicants respectfully note that in Korab there is no teaching of any low melting point compound in combination with a water soluble excipient to form a fast dissolve granulation.

Further, there is no motivation in Korab to replace the effervescent component or a portion of the effervescent component with a fast dissolve granulation to obtain a fast dissolve tablet.

The deficiencies of Korab are not cured by Mauger. Mauger is directed to a taste masking coating not to a tablet that dissolves readily see abstract, column 1, lines 56-65 and claim 1. As discussed above, the coating is a mixture of triglycerides and a polymer with the coating intended to remain intact until the tablet reaches the stomach (col. 2 lines 21-29). Arguably Mauger doesn't even teach a fast dissolve coating much less a fast dissolve tablet. Mauger teaches the use of low melting point compounds in combination with a polymer to form a coating that remains intact until the tablet gets to the stomach. Thus, Mauger neither teaches or suggests the elements needed to cure the identified deficiency of Korab - namely the combination of a water soluble excipient and a low melting point solid that forms a fast dissolving granulation.

Thus, there is no teaching or suggestion in Korab, Mauger or in the combination of Korab and Mauger of Applicants' invention of a combination of a water soluble excipient and low melting point to form a fast dissolving granulation. Further, there is no motivation in Korab's description of an effervescent composition

depending on chemical reaction for rapid disintegration and/or Mauger's coating to maintain a tablet intact until it reaches the stomach to form Applicants' fast dissolve granulation of a water soluble excipient and a low melting point solid.

In view of at least these distinctions and the fact that Applicants have amended independent Claim 1 to specify that the water soluble excipient and low melting point compound are a fast dissolve granulation, Applicants respectfully request that the Examiner withdraw the rejection of claims1-14 under 35 USC §103 over Korab et al. (US 5,178,878) in view of Mauger et al. (US 5,728,403).

Rejection Under 35 USC §103 – Makino

Claims 1-9 and 14 stand rejected under 35 USC §103 (a) over Makino (U.S. 5,501,861, herein "Makino"). Makino discloses a pharmaceutical preparation designed for buccal dissolution (see col. 2, lines 54-65) which is a compression molding of a carbohydrate, active agent, and a small amount of water that yields a "porous tablet ...capable of disintegration and dissolving rapidly in the oral cavity". As Makino discloses in column 5, lines 1-50 and column 6 lines 12-19, the key factors in creating the desired properties of the composition of Makino are the particle size of the carbohydrate, the proportion of carbohydrate to active, and the amount of water. No where in Makino is there any teaching or suggestion that a water soluble excipient combine with a low melting point compound will form a fast dissolve granulation nor is there any motivation provided to form a fast dissolve granulation as described by Applicants.

The addition of lubricants in Makino is optional (see col. 5, line 50 - col. 6, line 7), and the listing of lubricants include compounds such as, for example, talc and magnesium stearate which have melting points substantially above 37°C. Also, none of the 21 Examples provided by Makino appear to explicitly include any conventional lubricant. Accordingly, there is no teaching or suggestion in Makino of a low melting point compound that melts below 37°C in combination a with a water soluble excipient that together form a fast dissolving granulation.

Further Makino does not provide a reasonable expectation of success combining a low melting point compound with a water soluble excipient to from a fast dissolve granulation. In contrast to Applicants' fast dissolve granulation, Makino teaches that the critical factors in achieving fast dissolution are selection of the particle size of the carbohydrate, the proportion of carbohydrate to active, and the amount of water.

In view of at least these distinctions and the fact that Applicants have amended independent Claim 1 to specify that the water soluble excipient and low melting point compound are a fast dissolve granulation, Applicants respectfully request that the Examiner withdraw the rejection of claims 1-9 and 14 under 35 USC §103 over Makino.

CONCLUSION

In view of the amended claim set presented herein and the above remarks, Applicants respectfully request that amended claim 1 and claims 2-14 which depend from claim1 be allowed.

Should the Examiner believe that anything further is desired in order to place the application in even better condition for allowance, the Examiner is invited to contact Applicant's representative at 804-257-2544.

Respectively submitted,

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